Intraoperative assessment of biliary anatomy for prevention of bile duct injury

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REVIEW

Intraoperative assessment of biliary anatomy for prevention of bile duct injury: a review of current and future patient safety interventions

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Abstract

Background Bile duct injury (BDI) is a dreaded complication of cholecystectomy, often caused by misinterpretation of biliary anatomy. To prevent BDI, techniques have been developed for intraoperative assessment of bile duct anatomy. This article reviews the evidence for the different techniques and discusses their strengths and weaknesses in terms of efficacy, ease, and cost-effectiveness.

Method PubMed was searched from January 1980 through December 2009 for articles concerning bile duct visualization techniques for prevention of BDI during laparoscopic cholecystectomy.

Results Nine techniques were identified. The critical-view-of-safety approach, indirectly establishing biliary anatomy, is accepted by most guidelines and commentaries as the surgical technique of choice to minimize BDI risk. Intraoperative cholangiography is associated with lower BDI risk (OR 0.67, CI 0.61–0.75). However, it incurs extra costs, prolongs the operative procedure, and may be experienced as cumbersome. An established reliable alternative is laparoscopic ultrasound, but its longer learning curve limits widespread implementation. Easier to perform are cholecystocholangiography and dye cholangiography, but these yield poor-quality images. Light cholangiography, requiring retrograde insertion of an optical fiber into the common bile duct, is too unwieldy for routine use. Experimental techniques are passive infrared cholangiography, hyperspectral cholangiography, and near-infrared fluorescence cholangiography. The latter two are performed noninvasively and provide real-time images. Quantitative data in patients are necessary to further evaluate these techniques.

Conclusions The critical-view-of-safety approach should be used during laparoscopic cholecystectomy. Intraoperative cholangiography or laparoscopic ultrasound is recommended to be performed routinely. Hyperspectral cholangiography and near-infrared fluorescence cholangiography are promising novel techniques to prevent BDI and thus increase patient safety.

Keywords Cholecystectomy · CBD · Common bile duct · Complications

Abbreviations

BDI	Bile duct injury
LC	Laparoscopic cholecystectomy
CBD	Common bile duct
CVS	Critical view of safety
IOC	Intraoperative cholangiography
CCC	Cholecystocholangiography
LUS	Laparoscopic ultrasound
NIRF-C	Near-infrared fluorescence cholangiography

Cholecystectomy is one of the most frequently performed operations in the Western world, with over 750,000 yearly in the United States alone [1]. Bile duct injury (BDI) is a dreaded complication of cholecystectomy. When the

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laparoscopic technique was introduced in the early 1990s an increase of BDI was noted from approximately 0.2% to about 0.5% [2].

The burden of BDI on patients is considerable. Reinterventions through surgical, endoscopic, or radiologic procedures in specialist centers are frequently necessary [3–5]. BDI has low but finite short- and long-term mortality rates [6, 7]. A recent study reported that BDI had a significant negative effect on quality of life even 10 years after the event [8]. BDI is also associated with substantial financial burden for the health-care system: A British study calculated an average cost of 108,000£ ($\sim$175,000 $US) for major BDI (hospital and society costs). In addition, BDI is frequently grounds for malpractice litigation [7, 9, 10].

During laparoscopic cholecystectomy the primary cause of BDI is an error of visual perception (in 71–97% of cases), not insufficient technical skill of the surgeon [11, 12]. Factors that impede visual assessment and increase the risk of BDI include past or ongoing inflammation, variant ductal anatomy, and limited surgical experience [2, 13].

To prevent BDI, systematic safety interventions have been developed to provide insight into the biliary anatomy during cholecystectomy. For such an intervention to be effective, it first needs to be safe for patients and personnel. Second, it needs to be simple to use and easy to interpret since a wide range of surgeons and residents perform cholecystectomies. Third, considering the large volume of cholecystectomies and the continuous pressure to keep health-care expenditures under control, extra operating time, material expenses, and personnel expenses need to be kept to a minimum.

This review aims to provide an overview of the different modalities for intraoperative assessment of biliary anatomy during cholecystectomy and discuss their strengths and weaknesses.

Methods

The electronic database PubMed and the Web of Science were searched from January 1980 through November 2010 for English language articles concerning techniques of intraoperative assessment of biliary anatomy for prevention of BDI. The following search terms were used: "bile duct injury," "cholecystectomy," "intraoperative cholangiography," "cholangiography," "bile duct visualization," "bile duct imaging," and "bile duct mapping." The reference lists of the selected articles were also searched.

To portray the protective effect of conventional intraoperative cholangiography (IOC) on BDI in a forest plot, all studies of more than 10,000 patients were selected that explicitly compared the incidence of BDI in (laparoscopic) cholecystectomy with IOC to that without IOC. Studies that compared only the routine use of IOC with selective use were not included in the forest plot.

Microsoft Office Excel 2003 (Microsoft, Redmond, WA, USA) and SPSS v16.0 for Windows (SPSS Inc., Chicago, IL, USA) were used for the statistical analysis and to create the forest plot.

Results

The identified studies on the different imaging modalities are portrayed in Table 1.

Critical view of safety (CVS)

Although CVS is not an imaging modality per se, the operative technique plays a major role in establishing the anatomical orientation of the bile ducts and therefore needs to be discussed in this review.

Already in 1995, Strasberg et al. [14] described the "critical view of safety" (CVS) approach. Calot's triangle is dissected to achieve the following: First, one third of the gallbladder must be dissected free from the liver bed. Second, the triangle of Calot must be cleared (with liver segment V visible through the window). Third, the cystic artery and cystic duct must be the only two tubular structures remaining between the gallbladder and the hepatoduodenal ligament. In some cases, the cystic artery is diathermically dissected close to the gallbladder, in which case only the cystic duct remains to form the CVS. It is not necessary or recommended that the CBD be visualized. In this manner, the bile duct remaining can be none other than the cystic duct.

Achievement of the CVS is recorded in the operation report, preferably augmented by laparoscopic video or photographic images [15]. Failure to achieve the CVS is an absolute indication for conversion or additional bile duct imaging.

Four series, totaling close to 4,500 patients, have been published in which cholecystectomies have explicitly been performed using the CVS technique [16–19]. All four series showed very low BDI rates (0–0.03%). A Japanese review article noted a decrease in self-reported BDI during laparoscopic cholecystectomy from 0.77% in 2005 to 0.58% in 2007 and suggested that the increased implementation of the CVS technique played a role in this decrease [20]. Strasberg [21] mentioned the lack of level 1 evidence that the CVS approach prevents bile duct injury in his recent commentary.

Although undoubtedly a great step toward safer cholecystectomy, it is unclear whether the CVS alone is sufficient as a technique to minimize the risk of BDI. Our own

Table 1 Evidence on the different modalities for intraoperative assessment of the biliary tree

Primary author	No. of patients	Study description	Outcome
CVS—patient series of LCs using the CVS			
Rawlings [19]	54	All patients (suffering from biliary colic) underwent single-port LC using the CVS technique.	CVS in all patients; 0 BDI, 0 bile leaks
Sanjay [18]	447	All patients (acute pathology) underwent LC using the CVS technique.	CVS achieved in 388 (87%); 0 BDI, 0 bile leaks
Avgerinos [16]	1,046	All patients underwent LC using the CVS technique.	CVS achieved in 998 (95%); 0 BDI, 5 bile leaks (0.5%)
Yegiyants [17]	3,046	Administrative data of an institution in which CVS was standard. Injuries requiring surgical repair were identified.	CVS percentage not assessed; 1 BDI (0.03%), bile leaks not assessed
IOC—studies > 10,000 patients on the association between IOC and BDI			
Z'graggen [34]	10,174	1992–1995; analysis of LCs in a prospective database for which numerous Swiss institutions provide data (SALTS).	OR for BDI using IOC = 0.97 (95% CI 0.44–2.18), unadjusted for confounders
Flum [32]	30,630	1991–1998; Washington State Hospital Discharge Database searched for CBD repair codes <90 days after LC.	OR for BDI using IOC = 0.63 (95% CI 0.40–0.90), adjusted for confounders
Hobbs [30][a]	33,309	1988–1998; Western Australia Data Linkage System was searched in different ways for patients with complications. Medical files of these patients were assessed in detail.	OR for BDI using IOC = 0.68 (95% CI 0.42–1.03), adjusted for confounders
Flum [31]	1,570,361	1992–1999; US Medicare data was searched for codes for CBD repair within 1 year after cholecystectomy.	OR for BDI using IOC = 0.58 (95% CI 0.44–0.72), adjusted for confounders
Waage [33]	152,776	1987–2001; Swedish Inpatient Registry searched for codes for CBD repair within 1 year after cholecystectomy.	OR for BDI using IOC = 0.75 (95% CI 0.59–0.92), adjusted for confounders
Giger [35][b]	31,838	1995–2005; analysis of LCs in a prospective database for which numerous Swiss institutions provide data (SALTS).	OR for BDI using IOC = 1.14 (95% CI 0.76–1.70), unadjusted for confounders
LUS—patient studies on LUS during LC			
Machi [44]	2,159	Review of 12 studies (from before 1999) comparing LUS to IOC during LC.	Success of LUS and IOC 88-100%; BDI not assessed
Catheline [45]	600	All patients underwent LCs with LUS, 498 also underwent IOC.	LUS and IOC equal success; LUS faster (10 vs. 18 min, $P = 0.001$) BDI not reported
Kimura [49]	183	All patients underwent LCs with LUS and IOC.	LUS success 95%; IOC success 96%; 0 BDI; 1 bile leak after choledochotomy
Tranter [54]	367	All patients underwent LC with LUS.	LUS success 99%; BDI not reported
Biffl [46]	844	Nonrandomized comparison between LC with LUS ($n = 248$) and without LUS (594).	Without LUS: 11 BDI (1.9%); routine LUS: 0 BDI ($P = 0.04$)
Catheline [47]	900	All patients underwent LCs with LUS and IOC.	LUS success 100%; IOC success 85%; BDI not reported
Tranter [55]	135	All patients underwent LCs with LUS and IOC.	LUS success 97%, IOC success 90%; BDI not reported
Onders [52]	256	Description of one surgeon's experience with LUS.	Increase in use of LUS from 29% in 2001 to 77% in 2004; 0 BDI
Machi [50]	200	All patients underwent LC with LUS.	LUS success in 97%; 0 BDI, 0 bile leaks
Perry [53]	236	All patients underwent LC with LUS.	LUS success in 95%; 0 BDI; 0 bile leaks
Hakamada [48]	644	Comparison of outcome before ($n = 368$) and after ($n = 276$) introduction of routine LUS.	Without LUS: 4 BDI (1.1%); routine LUS: 0 BDI ($P = 0.08$)
Machi [51]	1,381	Prospective multicenter series of LC with LUS.	LUS success 98%; 0 BDI; 3 leaks (0.2%)
CCC—patient studies on CCC during LC			
Wills [58]	76	Randomized controlled trial between IOC ($n = 36$) and CCC ($n = 40$) during LC.	IOC success in 100%, CCC in 72% ($P < 0.001$); CCC images of poor quality
Daoud [59]	325	Nonrandomized comparison between IOC ($n = 35$) and CCC ($n = 290$).	IOC success 83%, CCC success 86%
Glattli [60]	69	Nonrandomized comparison between IOC ($n = 38$) and CCC ($n = 31$).	IOC success 92%, CCC success 48%; CCC images of inferior quality

Table 1 continued

Primary author	No. of patients	Study description	Outcome
Fox [61]	113	All patients underwent LC with CCC.	CCC was successful in 81%
Koksal [62]	40	All patients underwent LC with CCC.	CCC was successful in 90%
Moont [63]	97	All patients underwent LC with CCC.	CCC was successful in 85%
Young [64]	194	All patients underwent LC with CCC.	CCC was successful in 81%
Holzman [65]	60	Patients underwent "partial CCC" with the Kumar clamp.	Kumar CCC was successful in 83%
Kumar [66]	50	Patients underwent "partial CCC" with the Kumar clamp.	Kumar CCC was successful in 98%
Dye cholangiography—patient series on dye cholangiography during LC			
Pertsemlidis [67]	18	Indocyanine green (ICG) was intravenously administered to patients undergoing LC.	Cystic duct and CBD colored green in all patients. No images provided
Sari [68]	46	Blue dye was injected into the gallbladder during LC.	Cystic duct and CBD colored blue in 43/46 patients
Xu [69]	20	Blue dye was injected into the gallbladder during LC.	Extrahepatic bile ducts colored blue in 18/20 patients. No images provided
Light cholangiography—patient series			
Xu [69]	16	Optical fiber led into the CBD with a duodenoscope during LC. CBD cannulation successful in 13/16 patients.	CBD visualized in 13 cases, cystic duct only in 4 cases. No images provided
Passive infrared cholangiography—animal study			
Liu [70]	6 pigs	Room temperature saline was infused into the biliary tract. Images were taken with an infrared camera.	Infrared images correlated well with IOC. Artificial stones and BDI detected
Near-infrared cholangiography (NIRF-C)—patient studies on NIRF-C			
Mitsuhashi [73]	5	Open cholecystectomy after intravenous infusion of ICG. A NIRF camera system was used to capture images.	Fluorescence observed in the liver, gallbladder, and bile ducts of all patients
Ishizawa [71]	1	First laparoscopic experience with NIRF-C during cholecystectomy.	Fluorescence observed in cystic duct and CBD
Ishizawa [74]	10	Open cholecystectomy after intravenous infusion of ICG. A NIRF camera system was used to capture images.	Cystic duct and CBD were identified in 9/10 patients using NIRF-C
Aoki [75]	14	LC after intravenous administration of ICG.	CBD-cystic duct junction identified in 10/14 patients
Tagaya [76]	12	LC after intravenous ICG. Hepatoduodenal ligament was compressed with plastic device for improved exposure.	The CBD-cystic duct junction was identified in all patients
Ishizawa [86]	52	LC after intravenous ICG.	CBD-cystic duct junction identified in 50/52 patients
Hyperspectral cholangiography—animal studies			
Zuzak [82]	1 pig	A laparoscopic near-infrared, hyperspectral imaging system was used to assess bile duct anatomy in a pig.	Bile ducts, arteries, and veins all have unique reflectance spectra
Livingston [81]	8 pigs	Characteristics of different types of tissue were assessed using a laparoscopic hyperspectral imaging system.	Bile ducts, arteries, and veins all have unique reflectance spectra

LC laparoscopic cholecystectomy, *CVS* critical view of safety, *BDI* bile duct injury, *IOC* intraoperative cholangiography, *LUS* laparoscopic ultrasound, *CCC* cholecystocholangiography, *NIRF-C* near-infrared fluorescence cholangiography, *CBD* common bile duct, *ICG* indocyanine green, *OR* odds ratio

[a] Includes data set of Fletcher et al. [84]

[b] Includes data set of Krahenbuhl et al. [85]

data show occurrence of major BDI even after the CVS approach was adopted (unpublished). Also, major BDI continues to occur in the Netherlands despite increasing adoption of the CVS technique [4].

In spite of the lack of level 1 evidence, virtually all recent reviews, guidelines, and commentaries advocate the CVS technique [22–24]. Without an eligible alternative, the CVS should be regarded as the gold standard among *operative* techniques for assessment of biliary anatomy during laparoscopic cholecystectomy.

Intraoperative cholangiography (IOC)

Intraoperative cholangiography (IOC) is the most frequently applied technique for intraoperative assessment of the biliary anatomy. After dissection in Calot's triangle, the surgeon identifies and cannulates the cystic duct at the junction with the gallbladder. Radiographic contrast is then injected into the cystic duct and (subtracted) X-ray fluoroscopy images are obtained. The advent of dynamic fluoroscopy has improved the speed with which IOC can be performed and yields a series of high-resolution images that more accurately depict the biliary anatomy [25, 26]. IOC identifies whether the cannulated duct is indeed the cystic duct or mistakenly the CBD. In the latter case, the ductotomy may be repaired by inserting a T-tube and complete transection of the CBD is prevented. IOC may also identify abnormal biliary anatomy such as an accessory cystic duct or an aberrant right hepatic duct. IOC allows early detection of BDI, in which case a blush of contrast originating from the biliary tract or clips placed over the common or hepatic bile ducts may be seen. Quoted success rates are generally around or up to 90% [27, 28].

It has been calculated that a sufficiently powered, randomized controlled trial to assess the impact of IOC on BDI would need to include more than 30,000 patients [29]. As a result, the evidence of the role of IOC in the prevention of BDI consists mainly of population-based studies (Table 1). Figure 1 shows a forest plot of the six largest population-based studies (each >10,000 patients) [30–35] that compare the incidence of BDI in cholecystectomies explicitly performed using IOC to that in cholecystectomies explicitly performed without IOC. From this meta-analysis, the OR for BDI when using IOC was 0.67 (range = 0.61–0.75). When the studies were weighted according to actual size rather than the square root of the size, the OR was 0.60 (range = 0.52–0.70). Although the strongest evidence available, these studies are prone to bias and confounders as they rely heavily on administrative data of heterogeneous groups. For example, in these studies IOCs that were performed only because BDI was already suspected or observed, were included in the "IOC group." For this reason, the number of BDIs that occurred when IOC was used could have been substantially higher than the true incidence.

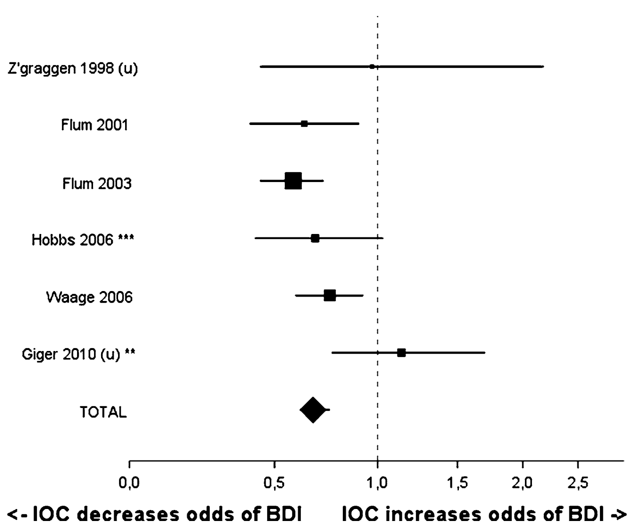

Fig. 1 Forest plot of protective effect of IOC on BDI during cholecystectomy [30–35]. *OR* odds ratio, *BDI* bile duct injury, *IOC* intraoperative cholangiography. *Unadjusted OR; **The data set of Fletcher et al. [84] is included in the study by Hobbs et al. [30]. ***The data set of Krahenbuhl et al. [85] is included in the study by Giger et al. [35]. Studies were weighted by the square root of the study size. Results are plotted on a natural logarithmic scale

Perhaps even more relevant than whether IOC in itself is useful is the question of whether it should be performed routinely or selectively. Metcalfe et al. [36] reviewed eight retrospective series of laparoscopic cholecystectomies (total of 6,024 patients) with routine IOC and nine series (3,268 patients) with a selective IOC policy. In this underpowered study, the rates of complete CBD transection were not significantly different, although a larger proportion of BDI was identified intraoperatively when routine IOC was used. Flum et al. [31], in their analysis of 1.5 million patients, found a lower incidence of BDI with surgeons who used IOC routinely: 0.43% vs. 0.51–0.54% ($P < 0.001$).

An important limitation of all the mentioned studies is that the cholecystectomies described took place mostly in the 1990s. During this era, the CVS technique was not yet widely implemented and therefore the studies can provide no information on the added value of IOC when the CVS technique is used. In our university hospital we retrospectively evaluated the implementation of a routine IOC policy in a population in which CVS was already the standard of care. We found 8/421 (1.9%) major BDIs before implementation of routine IOC versus 0/435 cholecystectomies after implementation of routine IOC ($P = 0.004$) (personal data). Although the CVS was the standard of care for all these patients, these data are limited in its retrospective nature.

In an editorial, Talamini [37] rightly pointed out that if the association between IOC and BDI is accepted to be causal, this will "radically alter the current practice of cholecystectomy."

Notwithstanding the association of IOC with lower BDI rates, it has several disadvantages which impede routine implementation. Cystic duct cannulation can be challenging, especially when it involves a short, thin, or brittle cystic duct, and the reported extra time needed for IOC is 10–27 min [38–40]. Special attention should be paid to the learning curve for interpreting IOC, as some studies report high proportions of incorrectly interpreted cholangiograms. For example, Way et al. [11] demonstrated that 34/43 (79%) routine cholangiograms that showed BDI were incorrectly interpreted. The radiation received during IOC is only around 0.18 mSv and represents a less than 0.001%

lifetime added risk of developing cancer [41]. Radiation exposure is therefore no argument against routine use of IOC in the adult population.

Another advantage of IOC is that the learning curve is generally short: a success rate of 95% was reached in an institution of eight supervising surgeons after 46 procedures [42]. Our own data, too, indicate a short learning curve: a success rate of 90% was reached in the first 3 months after implementation of routine IOC (personal data).

Whether routine IOC is cost effective depends on the estimated cost of IOC, the reduction of the BDI rate, and the cost to repair a BDI, patient death, and malpractice litigation. Flum et al. [43] entered varying estimates into cost-effectiveness models and concluded that if the relationship between IOC and lower BDI is indeed causal, routine application of IOC is cost effective.

In summary, there is a well-established relationship between IOC and lower incidence and increased early detection of BDI. It should be taken into account that these data are from before the CVS era and might not be extrapolated. Also, the sometimes cumbersome and time-consuming procedure limits the routine use of IOC in clinical practice.

Laparoscopic ultrasound (LUS)

An alternative to radiography for intraoperative assessment of biliary anatomy is laparoscopic ultrasonography (LUS). Laparoscopic flexible multifrequency ultrasound transducers with a Doppler flow detection system visualize tissue 4 cm in length and 6 cm in depth. The extrahepatic bile ducts may be scanned in the transverse and longitudinal planes. LUS can identify the CBD, the bifurcation cystic duct-CBD, hepatic artery, portal vein, inferior vena cava, and ampulla.

In 1999, Machi et al. [44] reviewed 2,059 patients who underwent both LUS and IOC and found a success rate of over 90% for both modalities. In the following years, extra evidence has been amassed on the value of LUS [45–55] (Table 1). Virtually all these studies report success rates of more than 95%, comparable to or higher than that of IOC. The intrapancreatic and intrahepatic parts of the biliary system are not always accurately depicted with LUS. The time needed for LUS ranges between 5 and 10 min.

One retrospective cohort study achieved significance in the main end point of BDI: 11/594 without LUS vs. 0/248 with LUS ($P = 0.04$) [46]. A prospective multicenter cohort study by Machi et al. [51] reported no BDI and only three bile leaks in 1,381 patients. The study of the ability of LUS to detect BDI intraoperatively is limited to two studies in pigs in which it successfully identified wrongfully placed clips and complete transections [56, 57].

All evidence shows excellent results with LUS in delineating the biliary anatomy. The advantages of LUS over IOC are the shorter procedure time, its noninvasive nature, and lack of use of radiation. Furthermore, it may be performed prior to dissection in Calot's triangle and repeated in uncertain cases. One of the main drawbacks of LUS is the reported long learning curve. Strangely, little data about this learning curve are available. Machi et al. [51] suggested that it takes 50–100 operations before one can successfully apply LUS. Although no efficient technique should be discarded simply because it takes time to learn, this does pose a limitation for the widespread implementation of LUS.

Cholecystocholangiography (CCC)

Cholecystocholangiography (CCC) is performed by injecting radiographic contrast directly into the gallbladder. An alternative instrument for "partial" CCC is the so-called "Kumar clamp," which is placed across the base of the gallbladder, after which radiographic contrast is injected into Hartmann's pouch.

The only randomized controlled trial found a lower success rate of CCC compared to IOC (72 vs. 100%, $P = 0.0005$) [58]. Also, CCC yielded inferior image quality and a 2.3 times longer radiation exposure. In comparative studies, Daoud et al. [59] reported comparable success rates for CCC and IOC, while Glattli et al. [60] found a very low success rate of 36% for CCC versus 90% in IOC. In general, success rates CCC series vary between 72 and 90% [61–64]. CCC reduces operative time compared to IOC [58]; times necessary to perform CCC are quoted as between 2 and 14 min [59, 61, 64]. The Kumar clamp for "partial" CCC was used in only two series, with success rates of 98 and 83% [65, 66]. The above-mentioned studies are further described in Table 1.

CCC is a simple technique with a steep learning curve [61], requires no cystic duct cannulation, and is faster than IOC. However, the success rate is low ($\sim$80%), and even when successful, the image quality is often poor. Of extra concern is the report of hypotension and gallbladder perforation when the gallbladder is distended [58]. Based on these arguments, CCC is not recommended as a standard procedure for cholangiography. An exception may be partial CCC using the Kumar clamp, as this instrument allows the injection of contrast under higher pressure and needs to fill only part of the gallbladder. However, this instrument has yet to prove its superiority to standard IOC.

Dye cholangiography

It has been reported that intravenous injection of high doses of indocyanine green (ICG) in patients undergoing LC color the extrahepatic bile ducts dark blue for 2 h [67]. Sari et al. [68] injected methylene blue directly into the gallbladder and were able to identify the gallbladder, cystic duct, and CBD in 43/46 cases (93%). Xu et al. [69] reported a success rate of 90% (18/20) (see also Table 1).

With dye cholangiography one has the advantage of being able to visualize the bile ducts prior to dissection. The technique is reasonably safe, although extravasation of the dye is not easily washed away and may obscure the view of the surgeon. The evidence for its effectiveness is limited. Xu et al. [69] indicated that the images obtained were of low resolution. None of the mentioned studies provide convincing images or quantitative data in support of the use of dye cholangiography. From a technical perspective, dyes in the visible light spectrum (380–600 nm) may not exhibit the necessary penetration necessary for a successful cholangiography, especially when Calot's triangle is filled and surrounded by fatty tissue or fibrosis resulting from a surpassed inflammatory process. This presents a serious limitation because it is in these particular cases that cholangiography has the greatest value.

Light cholangiography

Xu et al. [69] described an experimental technique called light cholangiography. An optic fiber is endoscopically passed up through the papilla of Vater and illuminates the extrahepatic duct system. Unfortunately, no images are provided, limiting the readers' ability to make a judgment on its clear merits.

Even if shown to be effective, light cholangiography done in this manner may be difficult to introduce as a routine procedure during laparoscopic cholecystectomy because it requires endoscopy with retrograde maneuvering of the optical fiber. Besides being time-consuming, this procedure is potentially hazardous, considering the reported morbidity and mortality associated with ERCP.

Passive infrared cholangiography

Liu et al. [70] experimented with a passive infrared camera. In nine pigs they infused room temperature saline or warm saline into the biliary tract, which contrasted with body temperature so that the biliary tract could be delineated (Fig. 2). Also, artificially created BDI and stones could be identified with this technique.

This method, which uses the brilliantly simple principle of small temperature differences, bypasses the ionizing radiation of IOC and can therefore take place repeatedly and in real time. However, it works only by direct infusion into the biliary system, as intravenous infusion would result in regression to body temperature within seconds. Moreover, the temperature of the saline within the bile duct may regress during the procedure necessitating repetitive injections. Therefore, infrared cholangiography is regarded as a suboptimal technique in the operating theatre.

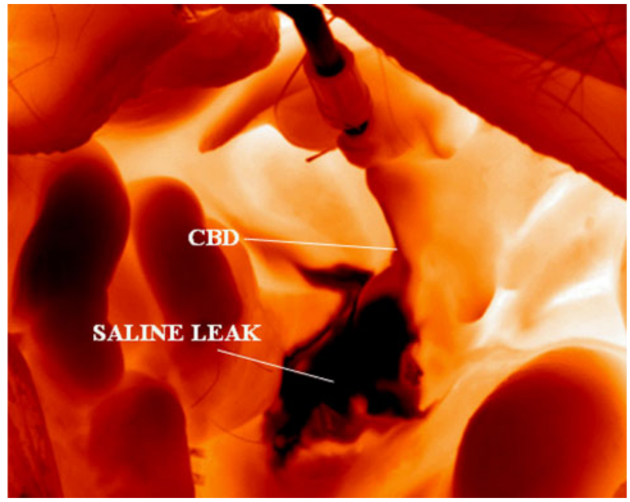

Fig. 2 Passive infrared cholangiography in a porcine model depicting leakage of room temperature saline from the common bile duct (CBD) [70] (with permission from Springer Science + Business Media, © 2008)

Near-infrared fluorescence cholangiography (NIRF-C)

In the past few years a new imaging modality has been tested for bile duct visualization: near-infrared fluorescence cholangiography (NIRF-C) [71]. This technique uses a laser to excite fluorescent agents and an imaging filter to register the light (of a slightly higher wavelength) that is subsequently emitted. Light in the NIRF spectrum (~800 nm) has optimal penetration and minimal absorbance and scattering in human tissue. Fluorophores cleared by the liver, such as indocyanine green (ICG) and IRDye® 800CW (LI-COR Biosciences, Lincoln, NE), may be administered intravenously or directly into the biliary system for imaging purposes.

After preliminary animal studies [72], NIRF-C has been used in a small number of patients since 2008 in open and laparoscopic (Fig. 3) cholecystectomy [71, 73–76]. Fluorescent signal was detected in the bile ducts of most patients, but the images were not very clear and had limited resolution. These studies are listed in Table 1. Figueiredo et al. [77] published high-quality images of detection of BDI in a mouse model, although their relevance was limited because of the absence of periductal fat in the mouse.

Very recently, Ishizawa et al. [78] published a larger series of 52 patients in whom laparoscopic near-infrared fluorescence images of a higher resolution than in a previous series were achieved. Eight preoperatively diagnosed accessory bile ducts were also visualized by NIRF-C.

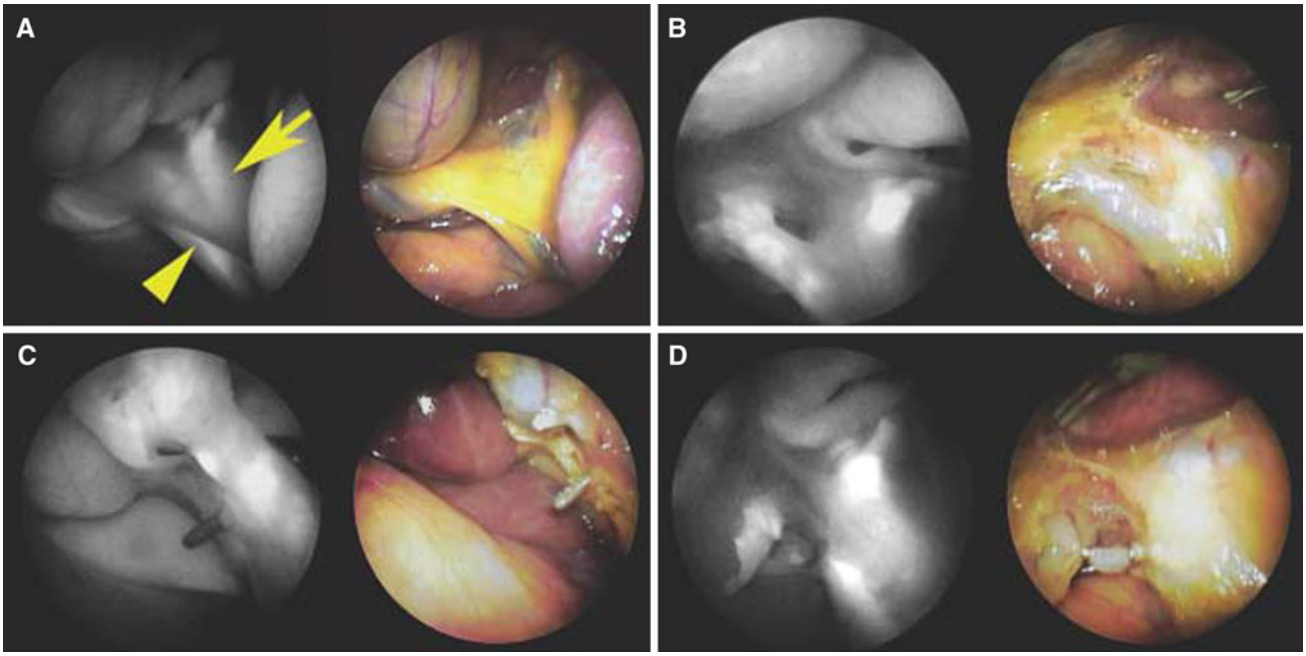

Fig. 3 Near infrared fluorescen cholangiography during laparoscopic cholecystectomy [78]. **A** Cystic duct running parallel to common hepatic duct, **B** isolation of cystic duct from anterior side of Calot's triangle, **C** isolation of cystic duct from posterior side of Calot's triangle, **D** closure of cystic duct (with kind permission from John Wiley and Sons Ltd © 2010, all rights reserved)

Although the authors, in a letter to the editor, stated that ICG is an excellent fluorophore, novel improved fluorophores will probably further increase the quality and resolution of the images. This is necessary to decrease the potential for misinterpretation of the fluorescence images, which is vital for widespread implementation of safety measures.

A multispectral NIRF imaging system, as recently described by Themelis et al. [79], simultaneously acquires real-time color and NIRF images of the operative field. A possible drawback of fluorescence imaging is the limited penetration depth. However, penetration up to 3 cm through medium resembling human adipose tissue has been described [80]. This depth is sufficient to visualize structures in Calot's triangle. NIRF-C is still in its experimental stage and images acquired are not as informative as IOC. However, properly developed using high-quality cameras and bile-cleared fluorophores, NIRF-C has the potential to be a simple-to-perform, easy-to-interpret, radiation-free, and personnel-sparing bile duct visualization technique.

Hyperspectral cholangiography

Livingston et al. [81] and Zuzak et al. [82] investigated the use of hyperspectral cholangiography in pigs. This method relies on different absorption and reflection patterns of different tissue (not upon excitation and emission as in fluorescence). The authors differentiate between gallbladder tissue and vascular tissue in pigs with a sensitivity and specificity of 98% [81]. Also, they processed the data into images that delineate the cystic duct in the hepatoduodenal ligament (Fig. 4) [82].

Hyperspectral cholangiography is appealing as it requires no exogenous contrast agent at all. Preliminary studies in pigs may be misleading as the porcine biliary system is often less obscured by fibrosis than is the human system. Validation studies in humans will need to take place before hyperspectral cholangiography may be considered a potential modality for intraoperative visualization of bile ducts.

Discussion

This article has provided an overview of the different modalities for intraoperative assessment of biliary anatomy, summarized in Table 2. The critical-view-of-safety (CVS) approach is considered the gold standard surgical technique to prevent BDI. As of yet, only a few published series were found in which achievement of CVS was specifically appraised. Although these studies suggest the protective effect of the CVS approach, future studies are necessary to appraise the effect of the CVS technique on BDI. Without an eligible alternative, and based on worldwide consensus, CVS should be regarded as the gold standard among *operative* techniques for assessing the biliary anatomy during laparoscopic cholecystectomy.

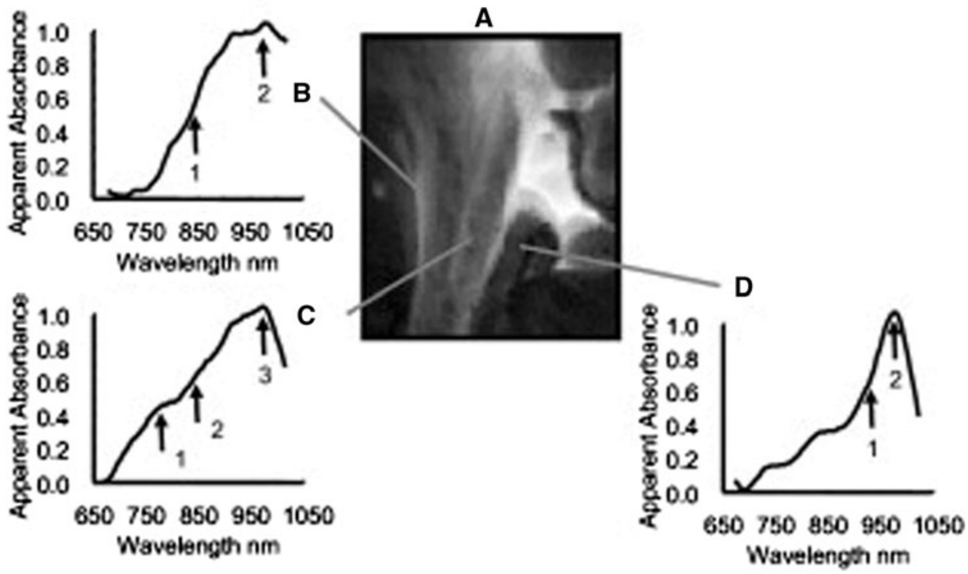

Fig. 4 Hyperspectral cholangiography. **A** Near-infrared (NIR) laparoscopic hyperspectral image of the hepatoduodenal ligament in live anesthetized pigs. **B** An artery indicated by spectra with broad oxyhemoglobin peak and a small water peak at 970 nm. **C** A vein is identified by spectra containing a deoxyhemoglobin shoulder, a broad oxyhemoglobin peak, and a small water peak. **D** The common bile duct is associated with spectra containing a lipid shoulder and a prominent water peak [82] (with permission from Elsevier Inc., © 2008)

Level 1 studies on conventional IOC have not been published [83], but the consistent large-cohort studies warrant a grade B recommendation. Further research will need to show the added value of IOC as the CVS technique gains acceptance. The inherent disadvantages of IOC cannot be denied: sometimes technically challenging cystic duct cannulation, need for X-ray equipment, prolonged operation time, and additional costs. Any developments in reducing these challenges, e.g., improvement in technology for the cannulation technique, would help the general surgeon accept performing routine IOC during cholecystectomy. Also, an appropriate financial incentive to perform IOC needs to be provided by the health-care insurance system to ensure regular use of this technique.

Many "outcome" studies (level 2c evidence [83]) support laparoscopic ultrasound (LUS) for prevention of BDI. The outcome is generally excellent, thus warranting a grade B recommendation. It should be kept in mind that the reported studies were executed in dedicated centers with experienced surgeons. As a consequence, their results cannot be automatically extrapolated to general surgical practices worldwide. However, in trained hands, LUS is at least as effective as IOC in defining biliary anatomy, and does so in less time and radiation-free. Failure of LUS to achieve wider acceptance probably lies within the presumed long learning curve.

Cholecystocholangiography, dye cholangiography, and light cholangiography may be dismissed as valid modalities for bile duct visualization. They either have too low a success rate, yield inferior images, or are too unwieldy for routine implementation. Passive infrared cholangiography may also prove too impractical for large-scale utilization.

The most promising novel developments in the field of bile duct visualization are NIRF-C and hyperspectral cholangiography. The main points to be proven in the future are whether they can provide sufficient anatomical resolution through the fatty fibrous tissue in Calot's triangle. With the development of more sensitive charge-coupled device camera systems and superior clinical-grade NIR fluorophores, these imaging modalities may provide the ideal tool for intraoperative bile duct imaging.

This review has focused solely on bile duct visualization for prevention and early detection of BDI. A second function of bile duct visualization is the detection of CBD stones during surgery. IOC and LUS are currently the only proven modalities for this clinical purpose. Some surgeons assess for stones only if there are clinical symptoms of cholestasis or abnormal liver function tests indicative of cholestasis, in which case a routine bile duct visualization modality does not necessarily need to convey information on the presence of stones.

In summary, the search is still ongoing for an optimal technique for intraoperative assessment of biliary anatomy that is safe, easy to perform, simple to interpret, personnel-sparing, cheap, and radiation-free. For now, we recommend that all surgeons use the critical-view-of-safety approach. Based on the available literature, it is recommended that intraoperative cholangiography or laparoscopic ultrasound of the biliary tree be performed routinely (grade B recommendation). In the future, hyperspectral cholangiography and near-infrared fluorescence cholangiography may prove

Table 2 Summary of techniques and modalities for intraoperative visualization of bile ducts

Modality	Application	Evidence	Safety	Ease	Success rate	Time
Critical view of safety (CVS)	–	Worldwide consensus that CVS technique is the gold standard for performing laparoscopic cholecystectomy, but limited evidence.	–	–	90–95%	–
Intraoperative cholangiography (IOC)	After dissection in Calot's triangle	Several very large retrospective data sets report association of IOC with lower rates of BDI.	Safe (minimally invasive)	At times cumbersome	90–95%	15 min
Laparoscopic ultrasound (LUS)	Repetitively	One retrospective study reported lower rates of BDI with LUS compared to no imaging modality. Many prospective studies report higher success rates of LUS than of IOC.	Very safe (noninvasive)	Requires considerable experience	>95%	5–10 min
Cholecystocholangiography (CCC)	Before dissection in Calot's triangle	One randomized controlled trial and several retrospective studies all show inferiority of images compared to IOC.	Reasonably safe (possible added risk of gallbladder rupture)	Easy	~80%	5–10 min
Dye cholangiography	Real time	Several series describe visualizing the biliary tract but convincing images and quantitative data are lacking.	Reasonably safe (risk of dye extravasation)	Easy	~90%	5–10 min
Light cholangiography	Real time	One series in patients is reported but no images are provided.	Potentially hazardous (retrograde maneuvering of an optical fiber into CBD)	Requires endoscopy skills	Unknown	Unknown
Passive infrared cholangiography	Real time	One study in pigs yielding excellent images.	Safe (minimally invasive)	Unknown	Unknown	Unknown
Near-infrared fluorescence cholangiography (NIRF-C)	Real time	Several animal studies yielding high-quality images of the biliary tract and BDI. A few small studies in patients yielding images of limited quality. One study of 52 patients with fair results.	Safe (noninvasive when intravenous agents are used)	Easy	Unknown	Unknown
Hyperspectral cholangiography	Real time	Two studies in pigs report positive differentiation between gallbladder tissue and blood vessel tissue.	Very safe (noninvasive)	Easy	Unknown	Unknown

BDI bile duct injury, *CBD* common bile duct

superior techniques for intraoperative visualization of the biliary anatomy.

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